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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/194,356	09/02/1999	DARIO NERI	515-4132	3100

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/194,356	NERI ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-47,53-55 and 57-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-37, 43-45, 47, 53-55 and 57-61* is/are rejected.

7)☒ Claim(s) *38-42 and 46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments and Amendments

1. Claims 30-47, 53-55 and 57-61 are pending.

Claims 30 and 43 have been amended.

Claim 56 has been cancelled.

Claims 59-61 have been added.

Claims 30-47, 53-55 and 57-61 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Sequence Compliance

3. The disclosure is objected to because of the following informality: it contains nucleic acid sequences with no accompanying identifying SEQ. ID. Numbers, see page 24, lines 15-17, 22 and 23. In order to fully comply with the sequence rules Applicants are required to insert SEQ. ID. Numbers, see MPEP 2421.02.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

4. The rejection of claim 47 under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention is withdrawn in light of Applicants' arguments and careful review

of IDS references (submitted February 8, 2005), Nilsson et al., reference number 82 and Santimaria et al., reference number 92

5. The rejection of claims 57 and 58 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Claim Rejections - 35 USC § 101

6. The rejection of claims 30-47, 53-55, 57 and 58 under 35 U.S.C. 101 because as written, do not sufficiently distinguish over antibodies as they exists naturally because claims 30-47 and 56-58 do not particularly point out any non-naturally occurring differences between the claimed antibodies and binding compositions and the structure of naturally occurring antibodies is withdrawn in light of the claim amendment. Claim 56 has been cancelled.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 30-37, 43, 55, 57, 59 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005. In anticipation of the instant rejection Applicants assert in the Remarks submitted February 14, 2005 that the Japanese application contains insufficient details and "there are insufficient details given of how the various types of FN are prepared...", see bridging paragraph of pages 7 and 8. Applicants also argue that the document does not contain proof that the asserted types of antibodies were obtained, see page 8, first full paragraph. These points of view and assertions have been carefully reviewed, but found unpersuasive.

JP(A) H2-76598 discloses a monoclonal antibody, which specifically recognizes the ED-B domain comprising 91 amino acids, see page 2, first and third paragraph. The disclosed antibody is referenced as OAL-CF525, see page 16, section B. The disclosure clearly notes "...figure [3] clarifies that the antibody of the present invention...reacts only with the cell type FN (nc and tc) and the fetus organ type FN (f).", see page 16, third paragraph.

The Japanese application did not indicate that the FN was treated with N-glycanase, consequently the said monoclonal antibody should bind to B-FN. The disclosed specific binding member when measured, as a purified monomer would inherently have a dissociation constant (Kd) of 6×10^{-8}M or less.

Applicants' arguments do not teach away or preclude the application of the instant art. Moreover, since the Patent and Trademark Office does not have the facilities for examining and comparing the disclosed antibody of JP(A) H2-76598 and

the antibody of the claimed invention the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the antibodies in the claimed invention and those of the prior art. See *In re Best*, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

8. Claims 30-37, 43, 47, 55, 57 and 59-61 are rejected under 35 U.S.C. 102(b) as being anticipated by JP(A) H4-169195 (laid open June 17, 1992)/ IDS reference number 24, submitted February 8, 2005. In anticipation of the instant rejection Applicants assert in the Remarks submitted February 14, 2005 that the Japanese application contains insufficient details and "there are insufficient details given of how the various types of FN are prepared...", see bridging paragraph of pages 7 and 8. Applicants also argue that the document does not contain proof that the asserted types of antibodies were obtained, see page 8, first full paragraph. These points of view and assertions have been carefully reviewed, but found unpersuasive.

JP(A) H4-169195 discloses a monoclonal antibody, which specifically recognizes the ED-B domain comprising 91 amino acids, see page 1, claim 2 and section 3 and page 4. The disclosed antibodies are referenced as OAL-pF115, OAL-TFN-01 and OAL-TFN-04, see page 18, last sentence; page 20, third paragraph. The disclosure clearly notes the antibodies of the present invention may be contained in art known carriers and pharmaceutical acceptable diluents, see page 20.

The Japanese application did not indicate that the FN was treated with N-glycanase, consequently the said monoclonal antibody should bind to B-FN. The disclosed specific binding member when measured, as a purified monomer would inherently have a dissociation constant (Kd) of 6 x 10^{-8}M or less.

Applicants' arguments do not teach away or preclude the application of the instant art. Moreover, since the Patent and Trademark Office does not have the facilities for examining and comparing the disclosed antibody of JP(A) H4-169195 and the antibody of the claimed invention the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the antibodies in the claimed invention and those of the prior art. See *In re Best*, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 30-37, 43-45, 55, 57-59 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005, in view of Bird et al. (Science 242:423-242,

1988). The teachings of the Japanese application have been discussed in the paragraphs above. The aforementioned reference does not teach that the antibody is single-chain Fv molecule (scFv) or a dimeric scFv.

However, Bird teaches the production of single-chain fragments, dimeric scFV and the efficacy of single-chain antibodies. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to produce single-chain antibodies. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in all references that single-chain antibodies are advantageous because of their small size, lower background in imaging applications, less immunogenic and ability to penetrate the microcirculation surrounding solid tumors better.

11. Claims 30-37, 43-45, 47, 55 and 57-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP(A) H4-169195 (laid open June 17, 1992)/ IDS reference number 24, submitted February 8, 2005, in view of Bird et al. (Science 242:423-242, 1988). The teachings of the Japanese application have been discussed in the paragraphs above. The aforementioned reference does not teach that the antibody is single-chain Fv molecule (scFv) or a dimeric scFv.

However, Bird teaches the production of single-chain fragments, dimeric scFV and the efficacy of single-chain antibodies. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to produce single-chain antibodies. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in all references that single-chain

antibodies are advantageous because of their small size, lower background in imaging applications, less immunogenic and ability to penetrate the microcirculation surrounding solid tumors better.

12. Claims 30-37, 43, 47 and 53-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005, in view of Bird et al. (Science 242:423-242, 1988), in view of Clackson et al. (Nature 352:624-628, August 15, 1991). The teachings of the Japanese application have been discussed in the 102(b) rejection. The aforementioned reference does not teach an antibody which is isolated from a synthetic molecular library.

However, Clackson teaches the production of single-chain fragments utilizing a random combinatorial library. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention by-passing hybridoma technology and animal immunization and using phage display creates produce single-chain antibodies, which are high-affinity antibodies. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in all references that single-chain antibodies are advantageous because of their small size, lower background in imaging applications, less immunogenic and ability to penetrate the microcirculation surrounding solid tumors better.

13. Claims 30-37, 43, 47, 54, 55, 57 and 59-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP(A) H4-169195 (laid open June 17, 1992)/ IDS reference

number 24, submitted February 8, 2005, in view of Clackson et al. (Nature 352:624-628, August 15, 1991). The teachings of the Japanese application have been discussed in the 102(b) rejection. The aforementioned reference does not teach a specific binding member which is isolated from a synthetic molecular library.

However, Clackson teaches the production of single-chain fragments utilizing a random combinatorial library. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention by-passing hybridoma technology and animal immunization and using phage display creates produce single-chain antibodies, which are high-affinity antibodies. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in all references that single-chain antibodies are advantageous because of their small size, lower background in imaging applications, less immunogenic and ability to penetrate the microcirculation surrounding solid tumors better.

14. Claims 30-37, 43, 53, 55, 57, 59 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable by JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005. The teachings of the Japanese application have been discussed in the 102 art rejection above. This reference does not teach a diagnostic kit comprising the antibody of claim 30.

Although the claims recite a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to form a

kit. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings well known in the art to place the recited oligonucleotides in a kit because it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, as well as the recited elements would provide an efficient mode of diagnosis.

15. Claims 30-37, 43, 53, 55, 57, 59 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable by JP(A) H2-76598 (laid open March 15, 1990)/ IDS reference number 23, submitted February 8, 2005. The teachings of the Japanese application have been discussed in the 102 art rejection above. This reference does not teach a diagnostic kit comprising the antibody of claim 30.

Although the claims recite a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to form a kit. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings well known in the art to place the recited oligonucleotides in a kit because it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy, as well as the recited elements would provide an efficient mode of diagnosis.

Allowable Subject Matter

16. Claims 38-42 and 46 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

17. Claims 38-42 and 46 are free of the art.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner works a flexible schedule, however she can normally be reached on 6:30 am to 5:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
16 March 2005